Journal Name

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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Phosphine-alkene ligand-mediated alkyl-alkyl and alkyl-halide elimination processes from palladium(II)†

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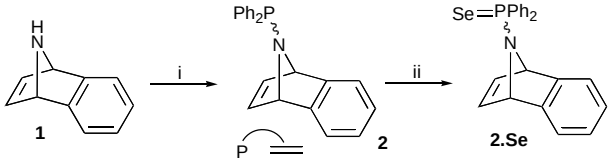
Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

***N*-Diphenylphosphino-7-*aza*-benzobicyclo[2.2.1]hept-2-ene (2) behaves as a chelating phosphine-alkene ligand for Pd^0 and Pd^{II}, promoting direct alkyl-alkyl and indirect alkyl-halide reductive elimination due to the stabilisation of the resulting *bis*(phosphine-alkene)Pd^0 complex.**

Palladium-mediated catalytic transformations are at the heart of contemporary synthetic organic chemistry, particularly for the controlled formation of C–C and C–heteroatom bonds.[1,2] Manipulation of these reactions necessitates a detailed understanding of the overall reaction trajectory and of the individual steps involved in the catalytic cycle. In particular, establishing factors that control reductive elimination from palladium is a key objective, since it is often through this step that final product formation occurs, *via* either a direct (four-coordinate) or indirect (three-coordinate) transition state.[3,4] The rate of reductive elimination is intimately linked to the nature of the coupling partners and to the palladium's ancillary ligands, with both steric and electronic factors playing a significant contribution in each case.[5] Significant effort has been devoted to studying the impact of a wide variety of ubiquitous monodentate phosphine and bidentate diphosphine metal scaffolds, with both their σ-donor character and chelate bite angle having been found to impact directly on elimination rates.[6,7,8,9]

Recently, efforts have begun to focus on the use of heteroditopic chelate ligands to increase control and further promote elimination. For example, a phosphine bearing a pendant electron deficient alkene has been shown to favour reductive elimination over a competing β-hydride elimination reaction pathway in Negishi cross-couplings.[10,11] The system's selectivity was attributed to the presence of the strongly π-accepting alkene moiety.

Since it is now well established that weakly *trans* influencing, poorly-donating/electron-accepting phosphines favour reductive elimination from Pd^{II}, we sought to explore the efficacy of a chelating phosphine-alkene (P-alkene) framework combining a weakly basic R_3P moiety with a strongly π-accepting alkene unit.[12,13,14] To this end, we describe here our use of a strained bicyclic 7-*aza*-norbornene motif to maximise Pd-to-alkene π-retrodonation through relief of ring strain.

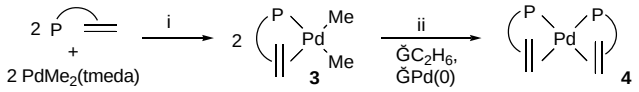


Scheme 1 Conditions: i) Ph_2PCl, NEt_3, CH_2Cl_2, –30 °C to r.t., 12 h, 69%; ii) Se, $CDCl_3$, r.t., 15 mins., 100%.

The ligand *N*-Ph_2P-7-*aza*-benzobicyclo[2.2.1]hept-2-ene (**2**) was prepared in 69% yield from 7-*aza*-benzobicyclo[2.2.1]hept-2-ene (**1**), *via* a straightforward nucleophilic substitution strategy, Scheme 1.[15,16,†] Compound **2** presents a single resonance by $^{31}P\{^1H\}$ NMR spectroscopy, $\delta^{31}P\{^1H\}$ 41.6 ppm, typical of an aminophosphine.[17] The barrier to inversion at nitrogen in compound **2** has been determined computationally (B3LYP/6-31G*) to be low, ~3 kcal mol^{-1} (*cf.* 16 kcal mol^{-1} computed for amine **1**), permitting **2** to adopt the necessary conformation for κ^2-*P*,*C* P-alkene metal chelation. The magnitude of $^1J_{Se\text{-}P}$ (792 Hz) for the phosphine-selenide **2·Se** confirms that the phosphorus donor moiety of **2** is weakly basic.[17,†]

To probe the ability of P-alkene **2** to enhance reductive elimination from Pd^{II}, its reaction with $PdMe_2$ and PdCl(Me) fragments has been explored. Treating a toluene solution of $PdMe_2$(tmeda) with one equivalent of compound **2** cleanly affords *cis*-[$PdMe_2$(κ^2-*P*,*C*-**2**)] (**3**), which exhibits a single resonance ($\delta^{31}P\{^1H\}$ 81.2 ppm), consistent with P-Pd binding. Coordination of the olefinic moiety is reflected in a shift to lower frequency of the alkene carbon resonance (**2**: δ 144.3 ppm; **3**: δ 119.2 ppm).

Complex **3** is thermally unstable in solution and over 5 days at r.t. smoothly evolves to afford half an equivalent of the monometallic Pd^0 complex [Pd(κ^2-*P*,*C*-**2**)$_2$] (**4**) (δ $^{31}P\{^1H\}$ +82.3 ppm) and ethane (δ ^1H 0.82 (s) ppm) as the only organic product, according to ^1H and ^{31}P NMR spectroscopy, accompanied by the precipitation of elemental palladium (Scheme 2).§ By comparison, complete thermolysis of [$PdMe_2$(dmpe)] is only achieved upon heating at 90 °C for 1 week,[18,19] highlighting the potential of ligand **2** in promoting reductive elimination processes.

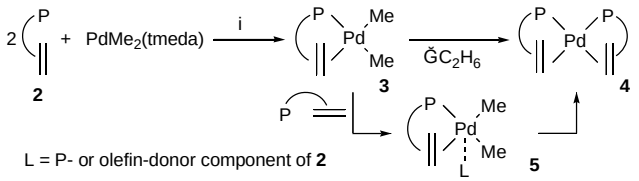


Scheme 2 Conditions: i) toluene, r.t., >99%; ii) toluene, r.t., 120 h, >99%.

The X-ray molecular structures of complexes **3** and **4** (Fig. 1)‡ confirm κ^2-*P,C* chelation of **2**. In complex **3** the palladium centre is planar, with one site occupied by the midpoint (Md) of the η^2-bound C(2)=C(3) bond, which is inclined by 88.3º to the coordination plane. The bond distances to palladium fall within the range observed for other complexes of the type *cis*-[$PdCl_2(\eta^2$-C=C)(PR_3)].[20,21,22,23,24] Consistent with moderate Pd→π*(C=C) retro-donation, the C(2)=C(3) bond in **3** (1.359(3) Å) is longer than the corresponding bond in an uncoordinated analogue of **2**, *N*-BOC-*aza*-benzonorbornadiene oxadisilole (1.315(4) Å).[25]

In complex **4**, the Pd coordination geometry is distorted-tetrahedral, with the Md-Pd-P planes of the two P-alkene ligands forming an 89.1° dihedral angle. Although the η^2-coordinated C=C bonds of **4** are longer (1.401(2) and 1.406(2) Å) than that of **3**, as would be expected, the difference is only moderate due to the comparatively poor π-donor character of d^{10} palladium species.[26]

If $PdMe_2$(tmeda) is treated instead with **2** in a Pd:**2** ratio of 1:2, much faster and quantitative formation of **4** is achieved (5 h, 20 ºC) consistent with rapid reductive elimination. Investigation of this reaction by variable temperature NMR spectroscopy (VT NMR) did not reveal any intermediates on the pathway from **3** to **4**. Consequently, we propose that the second equivalent of ligand **2** reacts with complex **3** to form a five-coordinate intermediate **5**, which then undergoes rapid reductive elimination to afford **4** (Scheme 3).



Scheme 3 Conditions: i) toluene, r.t., >99%.

The rate of reductive elimination from complex **5** is likely to be much greater than that from tetracoordinate complex **3** since prior reports have clearly established rate enhancements in reductive elimination with increasing coordination number.[27] The intermediacy of a five-coordinate species here is further supported by the observation that treating complex **3** with either 5 mol% of PPh_3 or propene both lead to a significant increase in the rate of reductive elimination of ethane, with formation of **4** being complete within 7 and 30 h, respectively, at 20 ºC (*cf.* 120 h in the absence of L-donor ligand).

To probe the role of the alkene moiety of **2** in promoting reductive elimination from **3**, the P-alkane ligand **6** (δ $^{31}P\{^1H\}$ 38.6 ppm), possessing an *aza*-norbornane rather than *aza*-norbornene framework, was prepared from *N*-BOC-7-*aza*-benzobicyclo[2.2.1]heptane.[28,]† Reaction of two equivalents of **6** with $PdMe_2$(tmeda) in toluene forms *cis*-[$PdMe_2(\kappa^1$-*P*-**6**$)_2$] (**7**), δ $^{31}P\{^1H\}$ 61.0 ppm, which cleanly isomerises to the *trans*-diphosphine complex **8** (δ $^{31}P\{^1H\}$ 59.7 ppm,) over a period of 24 h at 20 ºC (Scheme 4); no further reaction of **8** is observed even in the presence of excess **6** at 60 °C. Clearly κ^2-*P,C* chelation is vital in retaining the necessary *cis* geometry for reductive elimination from **3**.

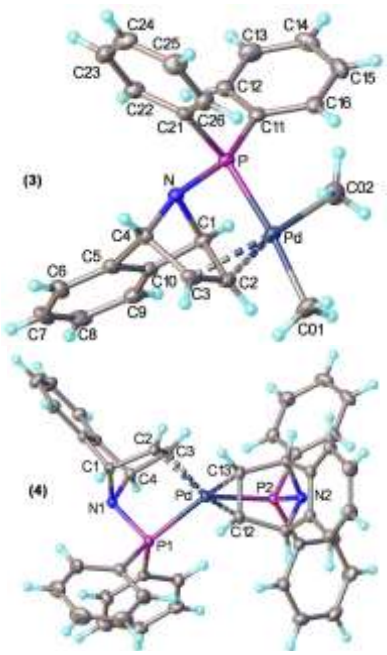
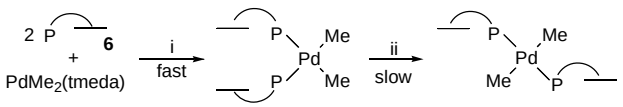
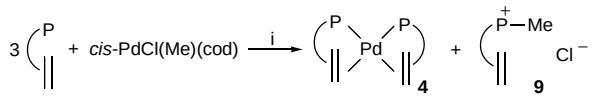


Fig. 1 X-ray molecular structures of **3** and **4**; thermal ellipsoids at 50% probability level. Selected bond distances (Å) in **3**: Pd−P 2.2876(6), Pd−C(01) 2.068(3), Pd−C(02) 2.074(3), Pd…C(2) 2.238(2), Pd…C(3) 2.266(2), P−N 1.732(2); in **4**: Pd−P(1) 2.3440(4), Pd−P(2) 2.3341(4), Pd…C(2) 2.1901(14), Pd…C(3) 2.1912(15), Pd…C(12) 2.2095(15), Pd…C(13) 2.1916(14), P(1)−N(1) 1.7470(13), P(2)−N(2) 1.7454(13).



Scheme 4 Conditions: i) toluene, r.t., >99%; ii) toluene, r.t., 24 h, >99%.

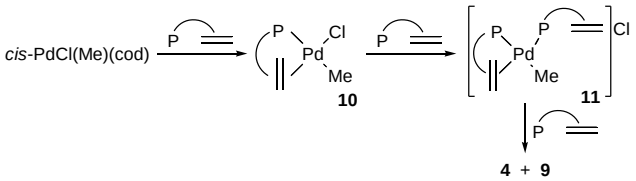
Due to significant M–Cl bond polarisation the barrier to alkyl chloride reductive elimination is much greater than that for alkyl-alkyl elimination; consequently, to the best of our knowledge no examples from Pd^{II} have been reported.[14] Therefore we were interested to probe whether P-alkene ligand **2** could also promote alkyl halide elimination. Notably, reaction of **2** with *cis*-PdCl(Me)(cod) (Pd:**2** = 1:1) does indeed give rise to Pd^0 complex **4** (consistent with reductive elimination), which is formed extremely rapidly (reaction complete within seconds at −40 °C according to VT NMR). However, **4** is obtained along with an equimolar quantity of **9** (δ $^{31}P\{^1H\}$ 38.1 ppm), the methyl phosphonium chloride salt of **2**, and leaving unreacted palladium starting material. In contrast, treating *cis*-PdCl(Me)(cod) with three equivalents of **2** rapidly and quantitatively affords a 1:1 mixture of **4** and **9** as the only products (Scheme 5).



Scheme 5 Conditions: i) toluene, r.t., >99%.

An analogous reaction of *cis*-PdCl(Me)(cod) with two or three

equivalents of the P-alkane ligand **6** (~5 mins, 20 °C) affords only *trans*-[PdCl(Me)(κ^1-*P*-**6**)$_2$] (**10**) (δ ^{31}P 6.7 ppm). To account for the formation of **4** and **9** it is proposed that initially [PdCl(Me)(κ^2-*P*,*C*-**2**)] (**10**) is formed, which undergoes rapid chloride ligand substitution (labilised by the *trans* alkene moiety[29]) by **2** to form complex **11**. In the presence of free ligand **2**, complex **11** then undergoes *pseudo*-reductive elimination affording phosphonium salt **9** and Pd^0 complex **4** (Scheme 6). Presumably, methyl-to-phosphorus migration is favoured here by the electron deficient nature of the amido-substituted phosphorus centre. Access to a pathway along which phosphonium salts may be generated is consistent with the formation of Ph_4PI having been observed following Heck coupling reactions involving [PdI(Ph)(PPh$_3$)$_2$] pro-catalysts.[30]



Scheme 6 Proposed pathway for the formation of phosphonium salt **9**.

In conclusion, by combining a readily prepared, poorly-donating phosphine component with a strongly π-accepting alkene moiety in a single bidentate ligand framework, **2**, it has been possible to efficiently promote reductive elimination from Pd^{II} complexes. The effectiveness of ligand **2** is attributed, in part, to its ability to form a stable *bis*(phosphine-alkene)Pd^0 complex, **4**, together with its *cis*-bidentate coordination. Notably, the inclusion of an electron poor phosphine moiety can also allow access to less common intramolecular *pseudo*-reductive elimination processes involving the coordinated phosphorus centre, resulting in phosphonium salt formation, in what can be regarded as a rare example of reductive elimination of chloromethane from Pd^{II}. Work is on-going to probe the utility of ligands such as **2** in a variety of catalytic applications.

Durham University and the EU (Marie Curie IE Fellowship to LB) are gratefully acknowledged for financial support. Johnson Matthey is thanked for the loan of palladium salts. Dr A.M. Kenwright and Mr I.H. McKeag are thanked for assistance with NMR spectroscopy. Acquisition of certain mass spectrometric data by the EPSRC National Mass Spectrometry Service at Swansea University is acknowledged.

Notes and references

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† Electronic supplementary information (ESI) available: experimental details and characterization data, including crystallographic data for **3** and **4**; computational studies. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/abcdefg

§ Integration of both the ^{1}H and ^{31}P[^{1}H] NMR spectra was quantified using an internal standard.

‡Bruker SMART 6000 CCD area detector, Mo-K_α radiation (λ=0.71073 Å), *T*=120 K, Olex2 software.[31] *Crystal data*: **3**, $C_{24}H_{24}NPPd$, *M*= 463.81, monoclinic, space group $P2_1/c$ (no. 14), *a*= 10.2185(3), *b*= 10.6113(4), *c*= 19.2717(7) Å, β=104.176(14)º, *U*= 2026.0(1) Å^3, *Z*=4, μ=1.00 mm^{-1}, 26057 reflections (2θ≤60º), R_{int}=0.061, *R*=0.031 on 4196 data with $I \geq 2\sigma(I)$, w$R(F^2)$=0.061 on all 5912 unique data. CCDC 894607. **4**, $C_{44}H_{36}N_2P_2Pd$, *M*= 761.09, triclinic, space group *P*-1 (No. 2), *a*=11.9327(6), *b*=12.2787(6), *c*=13.2937(6) Å, α=70.057(7), β=74.120(7), γ=81.517(7)º, *U*=1757.92(7) Å^3, *Z*=2, μ=0.65 mm^{-1}, 40908 reflections (2θ≤70º), R_{int}=0.038, *R*=0.036 on 11656 data with $I \geq 2\sigma(I)$, w$R(F^2)$=0.088 on all 14631 unique data. CCDC 894608.

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